SYNOPSIS

SYNTHESIS AND STUDIES OF SOME NEW HETEROCYCLIC COMPOUNDS OF MEDICINAL INTEREST

STUDIES ON HETEROCYCLIC COMPOUNDS

A great deal of research carried out in chemistry, is devoted to the study of heterocyclic chemistry. Heterocyclic chemistry is a branch which is inseparable from mankind origin or history because it provides our most of the basic need. The efficiency of heterocyclic compounds and its derivatives as pharmaceutical and agrochemical industries are well established. Heterocycles and their derivatives have attracted the attention of chemists mainly because of broad spectrum biological activities associated with this class of the compounds.

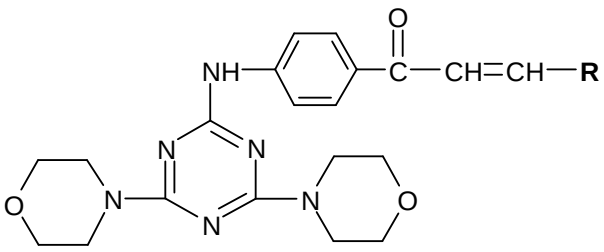
Heterocyclic compounds are cyclic compounds with ring containing carbon and other elements. The most common hetero atoms present in the ring are nitrogen, oxygen and sulphur. Heterocycles are those compounds with five or six membered heterocyclic ring which are stable, contain conjugated double bonds and exhibit aromatic character. The names of monocyclic compounds are derived by a prefix (or prefixes) indicating the nature of the hetero atoms present and eliding the 'a' where necessary, e.g. oxygen, oxa; sulphur, thia; nitrogen, aza; silicon, sila; phosphorus, phospha. When two or more of the same hetero atoms are present, prefixes di, tri etc… are used, e.g. dioxa, triaza. If hetero atoms are different, their order of naming will be O, S, N, P, Si e.g. thiaza (S then N).

Part – I STUDIES ON CHALCONES AND ITS DERIVATIVES

The chemistry of chalcones[1,2] has been recognized as a significant field of study. Chalcones are also known as benzal acetophenones or benzylidene acetophenones and were first coined by Kostanecki and Tambor[3]. Chalcones are coloured compounds because of the presence of the chromophore (-CO-CH=CH-). Chalcones have been found to possess many biological activities like analgesic[4], antitumour[5], antifeedant[6], antiplasmodic[7] antifungal[8] and antibacterial[9,10]. Chalcones are useful intermediates in the synthesis of various heterocyclic compounds such as pyrazolines, isoxazolines, pyrimidines, benzothiazepines, flavanones, isoxazoles and oxazepines etc… .

Synthesis and characterization of pyrazoline derivatives has been a developing field within the realm of heterocyclic chemistry for the past several decades because of their ready accessibility through synthesis and wide range of chemical reactivity. Pyrazoline derivatives have been found to possess wide range of therapeutic activities such as anticancer [11], antitubercular [12], anti-inflammatory[13,14] and antibacterial[15,16]. It has been reported that introduction of acetyl group at 1st position enhances the mollucicidal[17] activity as well as increases the stability of pyrazolines. Isoxazole derivatives have been reported to be active as anthelmintic[18], antileuckamia[19], antioxidant[20] and anti-inflammatory[21]. Pyrimidine derivatives play a vital role in many biological processes and in synthesis of many drugs. Many pyrimidine derivatives have displayed diverse pharmacological activities such as antibacterial[22-24], analgesic[25] and antifungal[26,27]. Substituted 1,5-benzothiazepine have been found to be effective for treatment of cancer[28] and promising anti-AIDS agents in preliminary screening[29]. Cyanopyridine derivatives have attracted considerable attention as they appeared of interest to possess anticancer[30], antibacterial[31,32], anti-inflammatory[33] and anticonvulsant[34] activities.

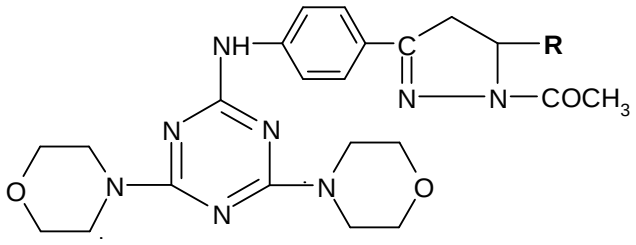
❖ In the present work, the condensation of different aromatic aldehydes and heterocyclic aldehydes with 2,4-bis-(tetrahydro-1',4'-oxazin)-6-(4'-acetylphenylamino)-*s*-triazine in the presence of alkali give chalcones **[I]**.



[I]

Where **R** = Phenyl / Substituted phenyl / Heterocyclic aldehydes

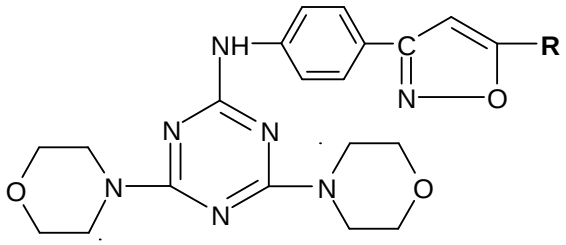
❖ Chalcones **[I]** on reaction with hydrazine hydrate in the presence of glacial acetic acid give acetyl pyrazolines **[II]**.



[II]

Where **R** = Phenyl / Substituted phenyl / Heterocyclic aldehydes

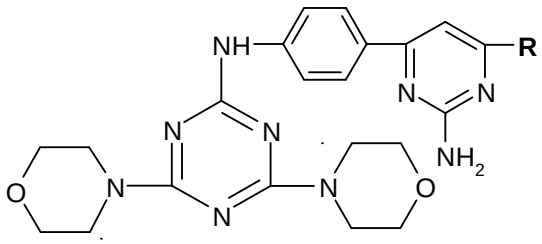
❖ Chalcones **[I]** on treatment with hydroxylamine hydrochloride in the presence of alkali give 2- isoxazoles **[III].**



[III]

Where **R** = Phenyl / Substituted phenyl / Heterocyclic aldehydes

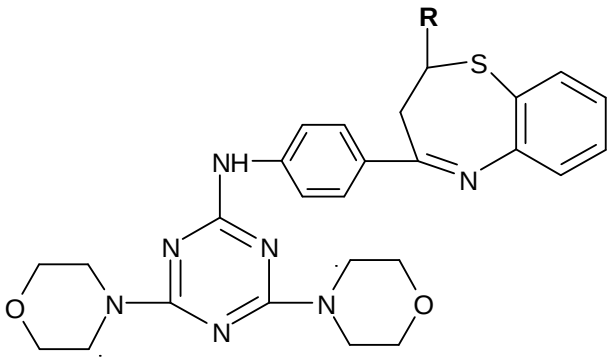
❖ Chalcones **[I]** on treatment with guanidine hydrochloride in the presence of alkali give 2-aminopyrimidines **[IV]**.



[IV]

Where **R** = Phenyl / Substituted phenyl / Heterocyclic aldehydes

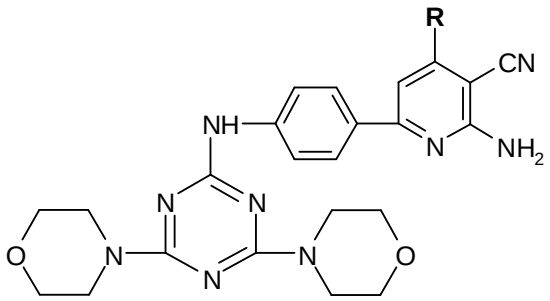
❖ Chalcones **[I]** on treatment with 2-aminothiophenol in the presence of glacial acetic acid give benzothiazepines **[V]**.



[V]

Where **R** = Phenyl / Substituted phenyl / Heterocyclic aldehydes

❖ Chalcones **[I]** on treatment with malononitrile in the presence of ammonium acetate give 2-amino-3-cyanopyridines **[VI]**.



[VI]

Where **R** = Phenyl / Substituted phenyl / Heterocyclic aldehydes

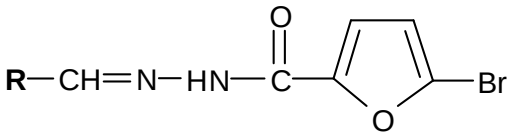
Part – II STUDIES ON THIAZOLIDINE-4-ONES

The Schiff-bases, in general are the condensation products of primary amines and aldehydes. They are represented by the general formula R-CH=N-R'. The N-substituted imines are often referred to as azomethines or anils. Schiff-bases have gained importance because of their physiological and pharmacological activities. The presence of azomethine (-CH=N-) linkage in Schiff-bases is responsible for the various biological activities such as antitubercular[35], antifungal[36] and antibacterial [37-39].

Thiazolidine-4-ones[40,41] have been reported to possess a wide range of pharmacological activities. Literature survey reveals that the various thiazolidine-4-ones have attracted considerable attention as they are endowed with wide range of pharmaceutical activities. Compounds containing thiazolidine ring exhibit variety of biological activities such as anti-HIV[42,43], antitubercular[44], anticancer[45], analgesic[46] and antimicrobial[47]. The presence of N-C-S linkage in the compound has been shown to have antioxidant[48] and antifungal[49] activities. Keeping the association of Schiff base and 4-thiazolidinone nucleus with various biological activities, it was contemplated to synthesised some Schiff-base and 4-thiazolidinone derivatives which have been described in the following sections.

Section - I

- In the present work, the condensation of 5-bromofuran-2-carbohydrazide with different aromatic and heterocyclic aldehydes to form Schiff-bases **[VII]**.

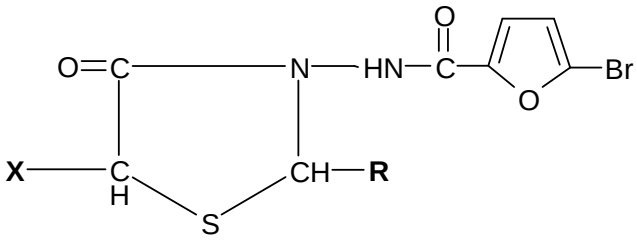


[VII]

Where **R =** Substituted aromatic and heterocyclic aldehydes

Section - II

- Schiff-bases **[VII]** on reaction with mercaptoacetic acid / merceptopropionic acid in dry toluene give corresponding 2,3-disusbstituted-thiazolidin-4-ones **[VIII]** / 2,3-disusbstituted-5-methyl-thiazolidin-4-ones **[IX]** .



[VIII] X = -H

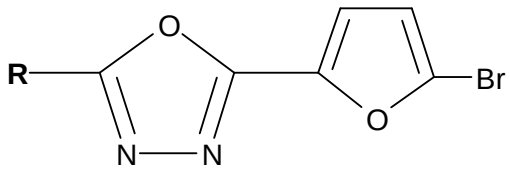
[IX] X= -CH_3

Where **R =** Substituted aromatic and heterocyclic aldehydes

Part – III STUDIES ON OXADIAZOLES

Oxadiazoles belong to an important group of heterocyclic compounds having toxophoric -N=C-O- linkage. It is only in the last decade that investigation in this field have been investigated due to their large number of application in the field of drug synthesis, dye stuff industry, heat resistant materials and heat resistant polymers. Oxadiazole derivatives have been found to possess anticonvulsant[50], hypoglycemic[51], antimicrobial [52] etc... .

In the present work, the condensation of 5-bromofuran-2-carbohydrazide with different aromatic and heterocyclic acid in $POCl_3$ give corresponding oxadiazoles **[X]**



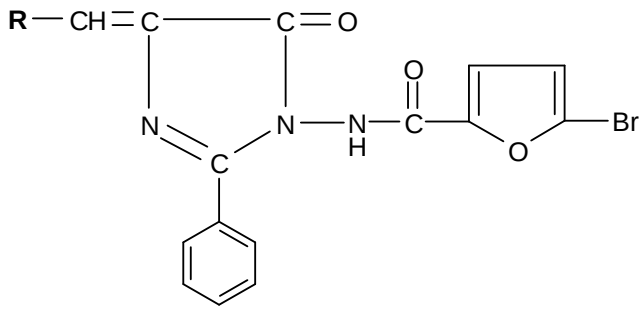
[X]

Where **R =** Substituted aromatic and heterocyclic acid

Part – IV STUDIES ON 5-IMIDAZOLONES

5-Imidazolones are biologically active[53-55] compounds. 5-Imidazolones are endowed with variety of pharmacodynamic activities such as antiallergic[56], antitubercular [57], anti-inflammatory[58] and antibacterial[59,60].

In the present work, the condensation of 5-bromofuran-2-carbohydrazide with 2-phenyl-4-(substituted benzylidene)-5-oxazolones in pyridine give corresponding 1-(5'-bromofuran-2'-carboxamido)-2-phenyl-4-(substituted benzylidene)-5-imidazolones **[XI]**. 5-Oxazolones were prepared by well known Erlenmeyer Azlactone synthesis [61].



[XI]

Where **R =** Substituted phenyl

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